REMARKS/ARGUMENTS

Upon entry of the instant amendment, claim 1 will be canceled without prejudice or disclaimer of the subject matter recited therein, and claims 2-8, 10-15 will be amended, whereby claims 2-92 will remain pending, with claims 2, 4, 16, 17, 18, 19, 28, 32, 38, 43, 48, 54, 59, 63, 67, 73, 78, 83 and 88 being independent claims.

Consideration Of Disclosure Statements

Applicants express appreciation for the inclusion with the Office Action of copies of the Forms PTO-1449 submitted with the disclosure statements filed July 16, 2001, October 3, 2001, November 3, 2001, November 28, 2001 and August 19, 2002, whereby the Examiner's consideration of these disclosure statements is of record.

Upon review of the Forms PTO-1449 attached to the Office Action, the following is noted.

(a) The Form PTO-1449 submitted with the disclosure statement filed November 5, 2001 which cites CHANG et al. is not initialed. Applicants are therefore submitting a Form PTO-1449 once again listing this document.

(b) The Form PTO-1449 submitted with the disclosure statement filed October 3, 2001 is apparently inadvertently not initialed at Citation No. 3 to LEIBOVICH et al.. Accordingly, Applicants are submitting a Form PTO-1449 once again listing this document.

(c) The Form PTO-1449 submitted with the disclosure statement filed July 16, 2001, on Sheet 2 of 10, has crossed out Citation No. 1 to BANERJEE, "Angiogenesis: Characterization of a Cellular Model", Puerto Rico Hlth. Sci., J., 17, 327-333. There is no indication as to why this document is crossed through. However, it is noted that a publication date is not included on the form. Applicants have presently included the publication date of January 1999 on the Form PTO-1449 submitted herewith.

(d) The Form PTO-1449 submitted with the disclosure statement filed July 16, 2001, on Sheet 4 of 10, has crossed out Citation No. 34 to KESSLER et al., "Mast Cells and Tumor Angiogenesis", Intern. J. Can., 18, 703-709 (1976) as being illegible. Applicants submit another copy herewith.

(e) The Form PTO-1449 submitted with the disclosure statement filed July 16, 2001 is apparently inadvertently not initialed at Sheet 6 of 10, Citation No. 55, Nguyen et al. Accordingly, Applicants are submitting a Form PTO-1449 once again listing this document.

Applicants respectfully request that the Examiner initial the Form PTO-1449 submitted herewith to indicate consideration of each of the documents. The Examiner is requested to forward an initialed copy of the form to Applicants with the next communication from the Patent and Trademark Office. If any fees are required in this connection, authorization is hereby provided to charge any required fee to Deposit Account No. 19-0089.

Formal Matters

Applicants respectfully request that the Examiner acknowledge the claim for domestic priority under 35 U.S.C. 119(e) to provisional Application No. 60/181,312.

Applicants request that the Request for Examiner Approval of Drawing Amendment filed September 12, 2001 be acknowledged, and that the drawing change requested therein be approved.

Response To Restriction Requirement

Applicants express appreciation for the rejoinder of Groups II and III with elected Group I, whereby the claims comprising the Groups I, II and III, i.e., claims 1-18, have been examined on the merits.

Applicants note that the restriction of Groups IV-XIV is maintained and has been made Final. Claims 19-92 stand withdrawn from further consideration pursuant to 37 C.F.R. 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Applicants are permitting non-elected claims 19-92 to remain pending subject to possible rejoinder upon allowance of the elected claims.

Response To Rejections Based Upon Prior Art

The following rejections are set forth in the Office Action:

(a) Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Presta et al. (hereinafter "Presta"), Cancer Research, Vol. 59, pp. 2417-24.

(b) Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Banerjee et al. (hereinafter "Banerjee"), Indian J. of Biochem. and Biophysics, Vol.. 30(6), pp. 389-94.

(c) Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banerjee, Indian J. of Biochem. and Biophysics, Vol.. 30(6), pp. 389-94.

In response to the rejections of record, Applicants respectfully submit the following.

Initially, Applicants note that Banerjee et al. has been cited as an Abstract by the Examiner on the Form PTO-892. Moreover, Banerjee et al. has been cited by Applicants in an Information Disclosure Statement filed July 6, 2001, and included on Sheet 5 of 10 as Citation No. 54 on the Forms PTO-1449 submitted therewith. Applicants assume that each of these documents is being utilized in the rejection, because the rejection does not specifically state which documents are being utilized.

As to the merits of the rejections, Applicants note that the claims have been amended and claim 1 has been canceled without prejudice or disclaimer of the subject matter recited therein, whereby the rejection based upon Presta is moot.

Regarding the rejections based upon Banerjee, Applicants respectfully submit that this disclosure by one of the present inventors does not teach or suggest the presently claimed invention. The disclosure set forth in Banerjee is directed to a study of dependence of protein N-glycosylation on capillary endothelial cell proliferation. The study indicates that amphomycin, a potent N-glycosylation inhibitor, inhibited capillary endothelial cell proliferation in a dose-dependent manner. The study is also stated to indicate that the β-agonist isoproterenol as well as other intracellular cAMP enhancing agents also enhance capillary endothelial cell proliferation.

It is also stated in the study that, in addition to cell proliferation, isoproterenol also enhanced protein glycosylation in these cells. It is noted in the study that isoproterenol effect was mediated by β-adrenoreceptors, as it got reduced on pre-treatment of cells with either atenolol or ICI 118, 551 or propranolol.

The study further states that isoproterenol stimulation of protein glycosylation by exogenous dolichyl monophosphate and its inhibition by tunicamycin (GlcNAc-1P transferase inhibitor) supported the concept that isoproterenol specifically stimulated protein N-glycosylation event(s) in the cell. Accordingly, tunicamycin is studied in Banerjee with respect to its effect on isoproterenol interactions, and not with respect to its effect on glycosylation and/or angiogenesis.

For example, at page 391 of Banerjee, the effect of amphomycin on endothelial cell proliferation and regulation of protein glycosylation by β-adrenoreceptor stimulation is studied. Moreover, Table 3 shows the effect of amphomycin on capillary endothelial cell doubling time and growth rate. In particular, Table 3 illustrates that at an increasing concentration of amphomycin, the growth rate (% over control) is decreased, whereby inhibition of growth is illustrated.

Following this discussion, Banerjee then discusses the effect of Dol-P, Dol-P plus tunicamycin, and propranolol on isoproterenol-mediated protein glycosylation with results being indicated in Table 6. Table 6 illustrates the effect of Dol-P, Dol-P + tunicamycin, and propranolol on isoproterenol-mediated protein glycosylation. As can be seen in the Table 6, there is measurement of the rate of mannose to leucine in the control and in isoproterenol treated cell. The study is aimed at the evaluation of isoproterenol, and utilizes differing materials in the study. There is no teaching or suggestion in this study of the presently claimed invention. The rejection cannot merely look to the occurrence of single words in a document, but must ascertain what the document teaches or suggests with respect to a combination of the words, and especially what the reference teaches as a whole. Under the present circumstances, Banerjee does not teach or suggest, Applicants disclosed and claimed invention. For example, Banerjee does not teach or suggest inhibiting angiogenesis using a nucleoside comprising glucosamine or a nucleoside comprising a pyrimidine nucleoside let alone tunicamycin and functional derivatives thereof.

Therefore, independent claim 2 patentably recites a method for inhibiting angiogenesis, comprising administering a nucleoside in an amount effective to inhibit angiogenesis, to a patient in need of such treatment, the nucleoside comprising glucosamine.

Dependent claim 3 further patentably defines that the glucosamine comprises N-acetylated glucosamine.

Independent claim 4 patentably defines that a method for inhibiting angiogenesis, comprising administering a nucleoside in an amount effective to inhibit angiogenesis, to a patient in need of such treatment, the nucleoside comprising a pyrimidine nucleoside.

Dependent claim 5 further patentably defines that the glucosamine comprises at least one of tunicamycin and functional derivatives thereof.

Dependent claim 6 further patentably defines that the glucosamine is represented by the recited formula.

Dependent claim 7 further patentably defines that the glucosamine comprises at least one of tunicamycin homologues A_1, A_2, B_1, B_2, C_1, C_2, D_1, and D_2.

Dependent claim 8 further patentably defines that the glucosamine is administered for a period of time, subsequently the administration of the glucosamine is suspended for a period of time of at least about 1 week, and subsequently the administration of the glucosamine is resumed.

Dependent claim 9 further patentably defines that the at least one of tunicamycin and functional derivatives thereof is administered for a period of time, subsequently the administration of the at least one of tunicamycin and functional derivatives thereof is suspended for a period of time of at least about 1 week, and subsequently the administration of the at least one of tunicamycin and functional derivatives thereof is resumed.

Dependent claim 10 further patentably defines that the glucosamine is administered for a period of about 1 week to 6 months.

Dependent claim 11 further patentably defines that the glucosamine is administered for a period of about 1 week to 6 months, subsequently the administration of the glucosamine is suspended for a period of about 1 week to 1 year, and subsequently the glucosamine is administered for a period of about 1 week to 6 months.

Dependent claim 12 further patentably defines that the glucosamine is administered daily in a dosage of about 5 to 20 mg/kg of body weight.

Dependent claim 13 further patentably defines that the glucosamine is administered for a period of about 1 week to 6 months at a daily dosage of about 5 to 20 mg/kg of body weight, subsequently the administration of the glucosamine is suspended for a period of about 1 week to 6 months, and subsequently the glucosamine is administered for a period of about 1 week to 6 months at a daily dosage of about 5 to 20 mg/kg of body weight.

Dependent claim 14 further patentably defines that the glucosamine comprises at least one of tunicamycin and functional derivatives thereof.

Dependent claim 15 further patentably defines that the patient in need of such treatment has at least one of diabetic retinopathy, atherosclerotic plaques, scleroderma, hypertrophic scarring, vascular adhesions, angiofibroma, trachoma graft neovascularization, corneal graft neovascularization, neovascular glaucoma, thrombosis, restenosis, osteoporosis, macular degeneration, arthritis, hemangiomas, psoriasis, and a tumor.

Dependent claim 16 patentably defines a method for inhibiting angiogenesis, comprising administering a nucleoside, which comprises glucosamine, in an amount effective to inhibit angiogenesis, to a patient in need of such treatment; wherein the nucleoside is administered for a period of time, subsequently the administration of the nucleoside is suspended for a period of time of at least about 1 week, and subsequently the administration of the nucleoside is resumed.

Dependent claim 17 patentably defines a method for inhibiting angiogenesis, comprising administering a nucleoside in an amount effective to inhibit angiogenesis, to a patient in need of

such treatment; wherein the nucleoside is represented by the recited formula; wherein the nucleoside is administered for a period of time, subsequently the administration of the nucleoside is suspended for a period of time of at least about 1 week, and subsequently the administration of the nucleoside is resumed.

Dependent claim 18 patentably defines a method for inhibiting angiogenesis, comprising administering tunicamycin in an amount effective to inhibit angiogenesis, to a patient in need of such treatment; wherein the tunicamycin is administered for a period of about 1 week to 6 months at a daily dosage of about 5 to 20 mg/kg of body weight, subsequently the administration of the tunicamycin is suspended for a period of about 1 week to 6 months, and subsequently the tunicamycin is administered for a period of about 1 week to 6 months at a daily dosage of about 5 to 20 mg/kg of body weight.

Applicants therefore respectfully submit that the prior art of record does not teach or suggest their disclosed and claimed invention. Accordingly, the rejections of record are without appropriate basis, and should be withdrawn.

CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections of record, and allow all the pending claims.

Allowance of the application is requested, with an early mailing of the Notices of Allowance and Allowability.

If the Examiner has any questions or wish to further discuss this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,
D. BANERJEE et al.

Arnold Turk
Reg. No. 33,094

August 20, 2003
GREENBLUM & BERNSTEIN, P.L.C.
1950 Roland Clarke Place
Reston, VA 20191
(703) 716-1191